REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 112, are respectfully requested in light of the following remarks.

Claims 37-40, 43, 44, 47, 53, 55-60, 62, 65, 66, 73-75, 77-80, 83 and 84 are under consideration. Claims 41, 42, 45, 46, 48-52, 54, 63, 64, 76, 81 and 82 have been withdrawn from consideration as being drawn to a nonelected species. Claims 67-72 and 85 have been withdrawn from consideration as being drawn to a nonelected group. Claim 61 has been cancelled. Claims 1-36 were previously cancelled.

Claim 37 has been amended to delete the phrase "low dose" from the preamble and to added "the active principle is located in the active layer but is not in the polymeric layer and the polymeric layer is present between the neutral support and the active layer, and the amount of said at least one active principle is less than 50 mg per tablet." Support for this amendment is found in the specification on page 1, lines 12-14 and page 3, lines 2-4. Claims 38-60, 62-67 and 73-84 have been amended to delete the phrase "low dose" from the preamble of the claims to have proper antecedent basis from claim 37 from which they depend. No new matter has been introduced as a result of the foregoing amendments.

Priority

Applicant thank the Examiner for noting that a certified copy of French application No 0313188 was not submitted.

A certified copy of French application No 0313188 is being requested and will be submitted when received by Applicant's representative.

Specification

The Office Action notes that trademarks have been used in the specification. Applicant notes that the trademarks were identified by the symbol ® and were accompanied by a generic description.

35 U.S.C. §112, Second Paragraph Rejection

Claims 37-40, 43, 44, 47, 53, 55-62, 65, 66, 73-75, 77-80, 83 and 84 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 previously recited the limitation of a "low dose". The remaining claims depend from claim 37. Claim 37 did not define "low dose" and therefore the metes and bounds for the amount of the material was unclear.

Claims 37-60, 62-67 and 73-84 have been amended to delete the phrase "low dose."

Claim 37 has been amended to recite that the amount of the at least one active principle is less than 50 mg per tablet. Applicant respectfully submits that claims 37-40, 43, 44, 47, 53, 55-60, 62, 65, 66, 73-75, 77-80, 83 and 84 particularly point out and distinctly claim the subject matter which applicant regards as the invention and therefore comply with the requirements of 35 U.S.C. §112, second paragraph. Applicant requests that this rejection be withdrawn.

35 U.S.C. §102(b) prior art rejections

1. Claims 37, 40, 59, 60-62, 78-80, 83 and 84 have been rejected under 35 3U.S.C. §102(b) as being anticipated by US Patent Application No. 2004/0242640.

It is well established that in order to demonstrate anticipation over 35 U.S.C. § 102(b), each feature of the claim at issue must be found, either expressly described or under principles of inherency, in a single prior art reference. See, *Kalman v. Kimberly-Clark Corp.*, 218 USPQ 789 (Fed. Cir. 1983).

The claims of the instant applications require that the active principle is located in the active layer but is not in the polymeric layer and that the polymeric layer is present between the neutral support and the active layer.

The '640 application teaches dual-release compositions of a COX-2 inhibitor. The Office Action states that the '640 application teaches an inert core which is coated with a first layer comprising HPMC and an analgesic and a second film coating comprising a sustained release polymer and an analgesic. (page 4, last paragraph) In both the first layer and the film coating, the analgesic is mixed with the polymer in the layer. The claims of the instant application require that the active principle is located in the active layer but is not in the polymeric layer and the polymeric layer is present between the neutral support and the active layer. The teachings of the '640 application, as stated by the Office Action, have the active principle in the polymeric layer, which is not permitted by the claims of the instant application. Therefore, the '640 application does not disclose each element required in the claims of the instant application.

Applicants therefore request the withdrawal of this rejection.

2. Claims 37, 39, 57, 59, 60, 62, 65, 73, 78 and 79 have been rejected under 35 3U.S.C. §102(b) as being anticipated by US Patent 5,783,215.

The '215 patent teaches a pharmaceutical preparation using controlled release beads containing a core around which a drug-containing layer is placed. The '215 patent teaches that the active compound thereby forms a compact layer together with the polymer on the insoluble core. (col. 3, lines 33-34) The '215 patent also teaches that "the method described above can be used for other pharmaceutical substances as well, provided that they can be dispersed in liquid containing a dissolved hydrophilic polymer." (col. 4, lines 1- 4)

The Office Action alleges that the '215 patent teaches an embodiment of a direct compression tablet formulation comprising an inert core covered with a hydrophilic polymer layer covered then with an active layer wherein the active layer comprises a hydrophilic polymer and a therapeutic agent. Applicant respectfully submits that the '215 patent does not teaches a hydrophilic polymer layer covering on the core which is then coated with an active layer wherein the active layer comprises a hydrophilic polymer and a therapeutic agent. The passage referenced by the Office Action states:

> According to the present invention the problem of mechanical suitability mentioned above has been overcome by using inert and non-soluble cores of glass or sand particles or soluble cores such as sugar spheres capable of withstanding mechanical stress, in combination with a plasticizing layer of a hydrophilic polymer containing the active substance, optionally with additional layers of the polymer not containing the active substance, layered between the core and the release controlling membrane. (col. 1, lines 31-40)

The above passage shows that the core is in combination with the layer of the active substance and the polymer. Thus any additional layers would need to be

applied over the layer of the active material and polymer. The optional additional layers of polymer not containing the active substance are a second layer that is applied over the first layer of the polymer and the active substance. This relationship is clearly shown in claim 1. There is nothing in the specification that teaches that a polymer layer not containing an active substance is coated onto the core before the layer of the active substance and the polymer is applied. The specification further teaches that the layer of active substance and polymer needs to be applied to the core by stating:

> When forming the pharmaceutical preparation according to the invention it has surprisingly been found that the addition of a hydrophilic polymer in a layer together with the active substance in specified ratios and the ratio of active substance to the core being within specified ratios in the beads, gives favourable mechanical properties withstanding cracking, especially of the release controlling membrane, when exposed to mechanical stresses, e.g. during filling in capsules or sachets or during compaction.
>
> The active substance is, according to the invention, dispersed in a solution of the hydrophilic polymer and applied to the core. By using powder layering, i.e. simultaneously spraying an aqueous solution of the hydrophilic polymer and the active substance as a drug powder onto the core, the principle according to the invention may be obtained. A solution of the active substance dissolved in a solvent may also be used, whereby the solution of active substance is applied onto the core. A release controlling membrane is further applied to obtain controlled release properties. This membrane may also contain additional polymers i.e. usable as coating materials for pharmaceutical purposes. (col. 2, lines 45-65)

The claims of the instant application require that a polymeric layer not containing the active ingredient be present between the core and the active layer. The '215 patent does not teach a polymeric layer not containing the active ingredient between the core and the active layer. Therefore, the '215 patent does not disclose each element required in the claims of the instant application.

Applicants therefore request the withdrawal of this rejection.

35 U.S.C. §103(a) Obviousness Rejection

1. Claims 37-40, 43, 44, 47, 53, 55-62, 65, 73-75, 77-80, 83 and 84 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,783,215 (the '215 patent) in view of U.S. Patent 6,607,751 (the '751 patent).

Applicants respectfully submit that these claims are not obvious over U.S. Patent 5,783,215 in view of U.S. Patent 6,607,751and that all of the claims are allowable.

To establish a *prima facie* case of obviousness, three basic criteria must be met. (MPEP 2143) First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teachings of the '215 patent were described above.

The Office Action alleges that the difference between the instant application and the '215 patent is that the '215 patent does not expressly teach xanthum gum as the hydrophilic polymer or glycerol fatty acid derivatives in the hydrophilic polymer layer. The Office Action relies on the '751 patent to overcome these alleged deficiencies. (page 7, last paragraph to page 8, line 2) The '751 patent teaches blending xanthum gum with the active ingredients, a polysaccharide and other excipients which are then granulated. The '751 patent does not relate to compositions having a core with a layer of a polymer and the active ingredient on the core.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There is no suggestion or motivation in the '215 patent and the '751 patent to modify the reference teachings to obtain the method of the applicants' invention. The '215 patent teaches forming a combination of a core with a layer comprising an active ingredient and a polymer. The '215 patent further teaches that problems with mechanical suitability were overcome using this combination. One of ordinary skill in the art would recognize that this passage teaches away from changing this feature. A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out it the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F3d 551, 553, 31 USPQ2d 1130, 1131. (Fed. Cir. 1994) One of ordinary skill in the art upon reading the '215 patent would not be motivated to change from using a composition in which a layer of an active compound and a polymer is placed on a core when the patent teaches that this element is needed to overcome problems associated with mechanical suitability. Absent some specific teaching, one of ordinary skill in the art would not make a change in an element that was fundamental in correcting a known problem. The Office Action has not cited any motivation to make such a change. Therefore, there is no suggestion or motivation, either in the cited reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference to obtain the invention of the instant application.

To establish a *prima facie* case of obviousness, there must be a reasonable expectation of success in obtaining the claimed method based modification of the cited prior art. The Office Action has not provided any information on the expectation of success in obtaining the claimed method based modification of the cited prior art. One of ordinary skill in the art upon reading the '215 patent would not believe that there was a reasonable expectation of success in changing a composition from one in which a layer of an active compound and a polymer is placed on a core to the currently claimed composition when the '215 patent teaches that this element is needed to overcome problems associated with mechanical suitability. As was shown above, the '215 patent teaches away from making the required modification to compositions in the '215 patent. There cannot be a reasonable expectation of success in making modifications contrary to elements taught to be necessary to overcome known problems absent some specific teaching to the contrary. Therefore there is no reasonable expectation of success in producing the applicants' invention based on the teachings in the cited prior art.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Neither the '215 patent nor the '751 patent teach or suggest a neutral support coated with a polymeric layer comprising at least one pharmaceutically acceptable polymer, and the polymeric layer coated with an active layer containing at least one active principle, wherein the active principle is located in the active layer but is not in the polymeric layer and the polymeric layer is present between the neutral support and the active layer. As was shown above, the '215 patent teaches a core of beads coated with a active substance containing layer which also contains a polymer. The

'215 patent teaches that the beads may comprise an outer release controlling membrane and that layers of polymer without an active substance may optionally be present. The structure of the composition in the '215 patent is distinct from the structure of the instantly claimed composition. Therefore, the prior art reference does not teach or suggest all the claim limitations.

For at least the above reasons, Claim 37 is patentable over the asserted combination of the '215 patent and the '751 patent. The remaining claims depend, either directly or indirectly, from Claim 37 and are, therefore, also patentable over the asserted combination of references for at least the reasons that Claim 37 is patentable. Reconsideration and withdrawal of the § 103(a) rejection over the combination of the '215 patent and the '751 patent is respectfully requested.

2. Claims 37 and 66 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,783,215 (the '215 patent) in view of U.S. Patent 6,607,751 (the '751 patent) as in the rejection above, and further in view of Gennaro.

Applicants respectfully submit that these claims are not obvious over U.S. Patent 5,783,215 in view of U.S. Patent 6,607,751 and further in view of Gennaro and that these claims are allowable.

The teachings of the '215 patent and the '751 patent were described above.

The Office Action alleges that the difference between the instant application and the combination of the '215 patent and the '751 patent is that the combination of the two patents does not expressly teach the tablets are scored.

The combination of Gennaro with the '215 patent and the '751 patent does not overcome the deficiencies noted above for the combination of the '215 patent and

the '751 patent. The comments provided above in the rejection based on the combination of the '215 patent and the '751 patent also apply to this rejection and have not been repeated to facilitate review by the Examiner.

Therefore Claims 37 and 66 are patentable over the asserted combination of the '215 patent, the '751 patent and Gennaro. Reconsideration and withdrawal of the § 103(a) rejection over the combination of the '215 patent, the '751 patent and Gennaro is respectfully requested.

3. Claims 37-40, 43, 44, 47, 53, 55-62, 65, 73-75, 77-80, 83 and 84 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,783,215 (the '215 patent) in view Damian et al. (European Journal of Pharmaceutical Sciences, vol. 10: 311-322), U.S. Patent 5,292,534 (the '534 patent), and Trinidade and Grosso (J. Microencapsulation, vol. 17(2): 169-176).

Applicants respectfully submit that these claims are not obvious over U.S. Patent 5,783,215 in view of Damian, U.S. Patent 5,292,534 and Trinidade and Grosso and that these claims are allowable.

The teachings of the '215 patent were described above.

The Office Action alleges that the difference between the instant application and the '215 patent is that the '215 patent does not expressly teach xanthum gum as the hydrophilic polymer or glycerol fatty acid derivatives in the hydrophilic polymer layer. The Office Action relies on Damian, U.S. Patent 5,292,534 and Trinidade and Grosso patent to overcome these alleged deficiencies. (page 11, last paragraph).

The combination of the cited references does not overcome the deficiencies noted above for the combination of the '215 patent and the '751 patent. The

comments provided above in the rejection based on the combination of the '215 patent and the '751 patent also apply to this rejection and have not been repeated to facilitate review by the Examiner.

Therefore Claims 37-40, 43, 44, 47, 53, 55-62, 65, 73-75, 77-80, 83 and 84 are patentable over the asserted combination of the '215 patent in view of Damian, U.S. Patent 5,292,534 and Trinidade and Grosso. Reconsideration and withdrawal of the § 103(a) rejection over the combination of the '215 patent in view of Damian, U.S. Patent 5,292,534 and Trinidade and Grosso is respectfully requested.

4. Claims 37 and 66 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,783,215 (the '215 patent) in view Damian et al. (European Journal of Pharmaceutical Sciences, vol. 10: 311-322), U.S. Patent 5,292,534 (the '534 patent), and Trinidade and Grosso (J. Microencapsulation, vol. 17(2): 169-176) as in the rejection above, and further in view of Gennaro.

Applicants respectfully submit that these claims are not obvious over U.S. Patent 5,783,215 in view of Damian, U.S. Patent 5,292,534 and Trinidade and Grosso and further in view of Gennaro and that these claims are allowable.

The teachings of these references were described above.

The Office Action alleges that the difference between the instant application and the combination of the '215 patent, Damian, the '534 patent and Trinidade and Grosso is that this combination of references does not expressly teach the tablets are scored.

The combination of '215 patent, Damian, the '534 patent and Trinidade and Grosso with the Gennaro does not overcome the deficiencies noted above for the

combination of '215 patent, Damian, the '534 patent and Trinidade and Grosso. The comments provided above in the rejection based on the combination of '215 patent, Damian, the '534 patent and Trinidade and Grosso also apply to this rejection and have not been repeated to facilitate review by the Examiner.

Therefore Claims 37 and 66 are patentable over the asserted combination of U.S. Patent 5,783,215 in view of Damian, U.S. Patent 5,292,534 and Trinidade and Grosso and further in view of Gennaro. Reconsideration and withdrawal of the § 103(a) rejection over the combination of U.S. Patent 5,783,215 in view of Damian, U.S. Patent 5,292,534 and Trinidade and Grosso and further in view of Gennaro is respectfully requested.

Double Patenting

Claims 37, 38, 43, 56-59, 61, 78, 79,83 and 84 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 3, 8-10, 14, 17 and 18 of copending Application No. 10/031,949 in view of U.S. Patent 5,783,215.

Applicants request that this matter be held in abeyance until such time as one of the applications is otherwise allowable. It is believed to be premature to file a terminal disclaimer before the scope of the claims has been settled. In the event that the Examiner is ready to allow this application except for this rejection, he is asked to contact the undersigned so that an appropriate terminal disclaimer can be promptly prepared and filed.

In view of the foregoing, it is believed that entry of the proposed amendments should be allowed and that the record rejections cannot be maintained against the proposed claims once entered into this application. Further, favorable action in the form of a Notice of Allowance is believed to be next in order and is earnestly solicited.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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